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PFHxS causes developmental hypothyroxinemia without affecting behavioral tests in offspring

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Introduction

Thyroid hormones (TH) are critical for mammalian brain development. In humans, low maternal serum thyroxine (T4) levels are associated with neurological deficiencies and cognitive impairment. Perfluorohexane sulfonate (PFHxS) is a widespread environmental contaminant found in human serum, tissues and milk. We have shown that PFHxS decrease serum thyroxine in pregnant rat dams and their offspring. Here, we further investigate effects on the thyroid system, neurodevelopment, and combination effects of PFHxS and a mixture of environmentally relevant endocrine disruptors.

Methods

Perfluorohexane sulfonate (PFHxS, 0, 0.05, 5 or 25 mg/kg/day with and without EDMix, a mixture of 12 endocrine disruptors e.g. phthalates, pesticides, UV-filters, Bisphenol A and butyl paraben) was administered (p.o.) to Wistar rat dams (n = 16-20/dose group) from gestation day (GD) 7 through postnatal day (PD) 22. Offspring were assessed in activity boxes and the radial arm maze.

Results/discussion

PFHxS not only decreased serum T4 levels in dams and offspring but in the high dose also reduced T3 to 84% of controls in both dams (PD 22) and pups (PD 16). The hypothalamic-pituitary-thyroid (HPT) axis was not activated based on lack of effect on serum TSH, thyroid gland histology, weight and thyroid gene expression levels. Developmental hypothyroxinemia did not appear to increase physical activity levels in young and adult offspring. However, the expected sex difference was absent on PD 115 in low dose PFHxS (0.05 mg/kg) and at high doses in combination with EDMix (5 mg/kg +EDMix and 25 mg/kg + EDMix). Slight effects on offspring learning and memory did not appear correlated to decreased TH levels during development.

Conclusions

PFHxS decreased circulating levels of T3 and T4 in pregnant rat dams and their offspring without apparent compensation by the HPT axis. The thyroid hormone disruption was not associated with detectable learning and memory deficits. Rather findings suggest that PFHxS may disrupt sexual differentiation of the brain. Standard behavioral assays appear insensitive to adverse effects on brain development caused by thyroid hormone disruption. Hence, there is a need for development of sensitive assays to protect human thyroid function. *Does not reflect EPA policy.*